REMARKS

Upon entry of the foregoing amendments, claims 16, 18-26, 29, and 39 are pending in the application. Claims 1-15, 32-33, 36, 38, and 44-45 have been canceled without prejudice. Claims 16 and 39 have been amended. Applicants submit that no new matter has been introduced by the amendments to the claims. The amended claims are fully supported by the specification as originally filed. Applicants further submit that the amendments and cancellations are made merely to expedite allowance of claims directed to most commercially relevant embodiments of the present invention. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants now address the Examiner's rejections in the order presented in the previous Office Action dated July 16, 2003.

Claim rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 4-15, 16, 18-26, 29, 39, and 45 are rejected under 35 U.S.C. § 112, first paragraph, on the ground that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Specifically, the Examiner takes the position that the specification, while "being enabling for an *in vitro* method of preferentially inhibiting proliferation of T cells or an *ex vivo* method of preferentially inhibiting proliferation of genetically engineered T cells in an animal, wherein in the *ex vivo* method introduced cells are autologous or allogeneic to the animal and wherein the mutated MBP in the *in vitro* or *ex vivo* methods have characteristics as recited in claim 1b and 1c, does not reasonably provide enablement for any other recited embodiments" (Office Action, page 2, lines 19-25). Further, the Examiner notes that "claim 16 is enabled for the scope stated above to the extent it encompasses the mutated MBPs recited in claim 1 with the characteristics recited in claim 1b and 1c" (Office Action, page 2, lines 29-31).

The basis of the rejection appears to have two components. (A) Applicants' claims drawn to *ex-vivo* gene therapy still encompass in-vivo considerations such as *in vivo* delivery of the nucleic acid encoding the mutated MBP. (B) Applicants' *ex vivo* method is enabled for

autologous or allogeneic cells only, not for xenogeneic cells. Applicants respectfully traverse this rejection to the extent that they are maintained in light of the amended claims.

(A) First, without acquiescing to the Examiner's assertion, Applicants have canceled claims 1-15, 32-33, 36, 38, and 44-45 and amended claims 16 and 39, without disclaimer or prejudice, to focus on aspects of greatest current commercial interest. Applicants submit that the rejection to claims 1, 4-15, and 45 is rendered moot in view of the cancellation of these claims. In addition, Applicants have adopted the Examiner's suggestion and amended claims 16 and 39. As amended, claims 16 and 39 encompass the mutated MBPs recited in claim 1 with the characteristics recited in claim 1(b) and 1(c). The amended claims 16 and 39 encompass *ex vivo* methods of engineering T cells to contain a nucleic acid encoding the mutated MBP. Applicants note that claims 16(b) and 39(b) have been amended to clarify the characteristics of the mutated MBPs. Support for these amendments are supported by the specification (e.g., page 2, lines 1-7) and the original claim 1.

(B) Second, Applicants traverse the ground of rejection related to xenogeneic cells, and respectfully request the Examiner's reasoning why the claimed invention is allegedly not enabling for xenogeneic cells while being enabling for autologous and allogeneic cells. Applicants point out that the specification clearly teaches how to make and use the invention as claimed. For example, "[T]he cells can be autologous cells, syngeneic cells, allogenic cells and even in some cases, xenogeneic cells. The cells may be modified by changing the major histocompatibility complex ("MHC") profile, by inactivating b_2-microglobulin to prevent the formation of functional Class I MHC molecules, inactivation of Class II molecules, providing for expression of one or more MHC molecules, enhancing or inactivating cytotoxic capabilities by enhancing or inhibiting the expression of genes associated with the cytotoxic activity, or the like" (page 31, lines 19-25).

Applicants also provide post-filing evidence (Poznansky et al., 2000, Nature Biotech, 18:729-734, enclose herewith as **Exhibit A**) demonstrating that xenogeneic cells can be employed for *ex vivo* gene therapy. Poznansky et al. describe that co-culture of the xenogeneic murine thymic stroma with human bone marrow-derived hematopoietic progenitor cells successfully generated mature functional T cells. In view of the teachings of the specification and the post-filing data, Applicants submit that one skilled in the art would have no problem

beyond the realm of routine experimentation in making and using the invention as claimed at the time when the application was filed.

For the above reasons, Applicants submit that the pending claims are in fact amply enabled by the teachings of the specification when considered in light of the knowledge of one of skill in the art as of the effective filing date. Therefore, reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, first paragraph is respectfully requested.

Claim rejection under 35 U.S.C. § 102

Claims 32, 33, and 44 are rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Futer et al. and Kawamura et al. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Without acquiescing to the Examiner's assertion, Applicants have canceled claims 1-15, 32-33, 36, 38, and 44-45, without disclaimer or prejudice, solely to focus on aspects of greatest current commercial interest. Applicants reserve the right to pursue the claims of similar or differing scope in the future. Therefore, the rejection of claims 32, 33, and 44 under 35 U.S.C. § 102 is rendered moot in view of the cancellation of these claims.

Claim rejection under 35 U.S.C. § 103

Claims 32, 33, 36, 38, and 44 are rejected under 35 U.S.C. § 103(a) as being allegedly obvious over Futer et al. or Kawamura et al. in view of Frutman et al. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

As described above, Applicants have canceled these claims, without disclaimer or prejudice, solely to focus on aspects of greatest current commercial interest. Applicants reserve the right to pursue these claims of similar or differing scope in the future. Therefore, the rejection of claims 32, 33, 36, 38, and 44 under 35 U.S.C. § 103 is rendered moot in view of the cancellation of these claims.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims as amended are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

Respectfully Submitted,

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